

What is claimed is:

1. A method for treating or preventing a neoplasia disorder in a mammal in need of such treatment or prevention, which method comprises administering to said mammal a therapeutically-effective amount of a combination of an integrin antagonist and one or more antineoplastic agents, wherein said antineoplastic agents are selected from the group consisting of anastrozole, calcium carbonate, capecitabine, carboplatin, cisplatin, Cell Pathways CP-461, cyclophosphamide, docetaxel, doxorubicin, etoposide, fluorouracil (5-FU), fluoxymestrine, gemcitabine, goserelin, irinotecan, ketoconazole, letrozol, leucovorin, levamisole, megestrol, mitoxantrone, paclitaxel, raloxifene, retinoic acid, tamoxifen, thiotepa, topotecan, toremifene, vinorelbine, vinblastine, vincristine, selenium (selenomethionine), ursodeoxycholic acid, sulindac sulfone and eflornithine (DFMO).
2. The method of Claim 1 wherein the combination is administered in a sequential manner.
3. The method of Claim 1 wherein the combination is administered in a substantially simultaneous manner.
4. The method of Claim 1 wherein the antineoplastic agent is capecitabine.
5. The method of Claim 1 wherein the antineoplastic agent is carboplatin.
6. The method of Claim 1 wherein the antineoplastic agent is cisplatin.

7. The method of Claim 1 wherein the antineoplastic agent is Cell Pathways CP-461.

8. The method of Claim 1 wherein the antineoplastic agent is docetaxel.

5 9. The method of Claim 1 wherein the antineoplastic agent is doxorubicin.

10. The method of Claim 1 wherein the antineoplastic agent is etoposide.

10 11. The method of Claim 1 wherein the antineoplastic agent is fluorouracil (5-FU).

12. The method of Claim 1 wherein the antineoplastic agent is fluoxymestrine.

13. The method of Claim 1 wherein the antineoplastic agent is gemcitabine.

15 14. The method of Claim 1 wherein the antineoplastic agent is goserelin.

15. The method of Claim 1 wherein the antineoplastic agent is irinotecan.

20 16. The method of Claim 1 wherein the antineoplastic agent is ketoconazole.

17. The method of Claim 1 wherein the antineoplastic agent is letrozol.

18. The method of Claim 1 wherein the antineoplastic agent is leucovorin.

25 19. The method of Claim 1 wherein the antineoplastic agent is levamisole.

20. The method of Claim 1 wherein the antineoplastic agent is megestrol.

30 21. The method of Claim 1 wherein the antineoplastic agent is mitoxantrone.

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22. The method of Claim 1 wherein the antineoplastic agent is paclitaxel.

23. The method of Claim 1 wherein the antineoplastic agent is raloxifene.

5 24. The method of Claim 1 wherein the antineoplastic agent is retinoic acid.

25. The method of Claim 1 wherein the antineoplastic agent is tamoxifen.

10 26. The method of Claim 1 wherein the antineoplastic agent is thiotepa.

27. The method of Claim 1 wherein the antineoplastic agent is topotecan.

28. The method of Claim 1 wherein the antineoplastic agent is toremifene.

15 29. The method of Claim 1 wherein the antineoplastic agent is vinorelbine.

30. The method of Claim 1 wherein the antineoplastic agent is vinblastine.

20 31. The method of Claim 1 wherein the antineoplastic agent is vincristine.

32. The method of Claim 1 wherein the antineoplastic agent is selenium (selenomethionine).

33. The method of Claim 1 wherein the antineoplastic agent is sulindac sulfone.

25 34. The method of Claim 1 wherein the antineoplastic agent is ursodeoxycholic acid.

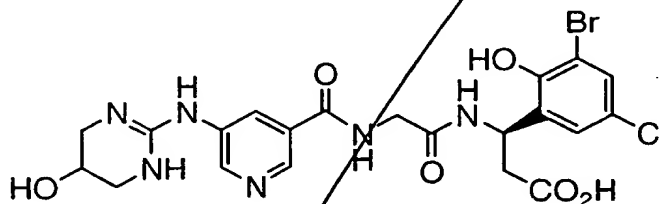
35. The method of Claim 1 wherein the antineoplastic agent is eflornithine (DFMO).

30 36. The method of Claim 1 wherein the integrin antagonist is selected from compounds, and their

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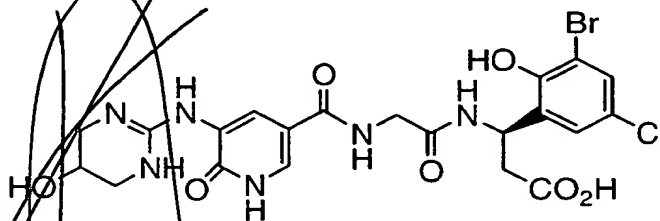
pharmaceutically acceptable salts thereof, of the group consisting of:

1)



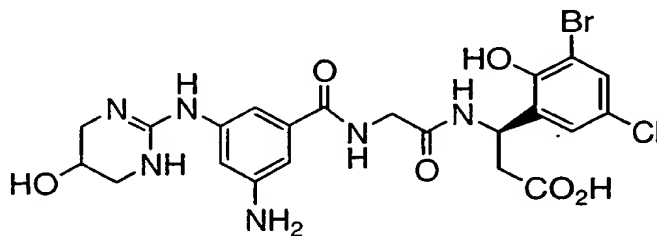
5 (3R)-N-[[5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-D-alanine,

2)



10 (3R)-N-[[1,6-dihydro-6-oxo-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-D-alanine,

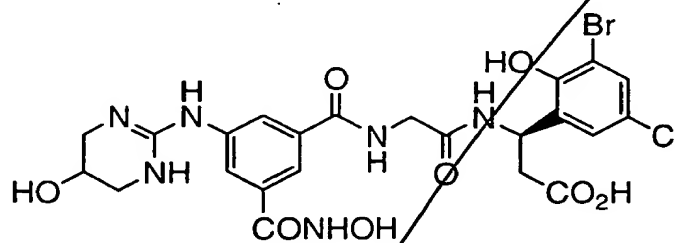
15 3)



(3R)-N-[3-amino-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-D-alanine,

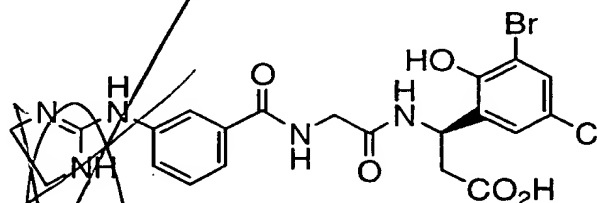
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4)



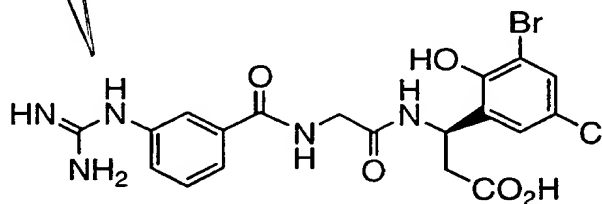
(3R)-N-[3-[(hydroxyamino)carbonyl]-5-
[(1,4,5,6-tetrahydro-5-hydroxy)-2-
pyrimidinyl]amino]benzoyl]glycyl-3-(3-bromo-5-
chloro-2-hydroxyphenyl)-b-alanine,

5)



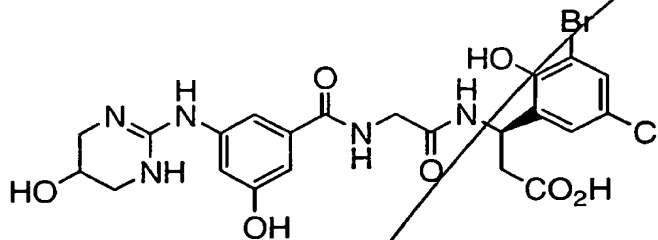
(3R)-N-[3-[(4,5-dihydro-1H-imidazol-2-
yl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-
hydroxyphenyl)-b-alanine,

6)



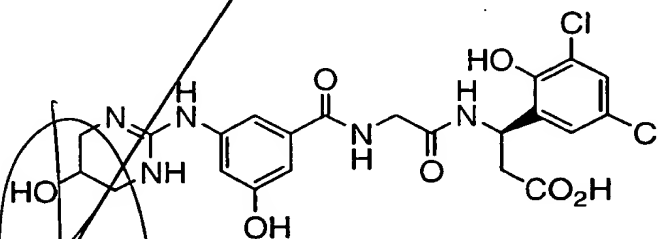
(3R)-N-[3-
[(aminoiminomethyl)amino]benzoyl]glycyl-3-(3-
bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

7)



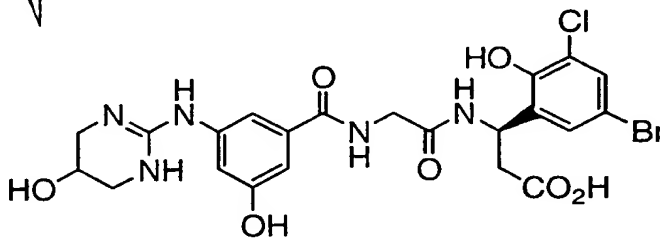
(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-L-alanine,

8)



(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3,5-dichloro-2-hydroxyphenyl)-L-alanine,

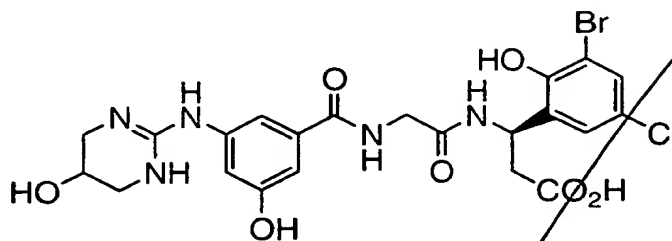
9)



(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(5-bromo-3-chloro-2-hydroxyphenyl)-L-alanine,

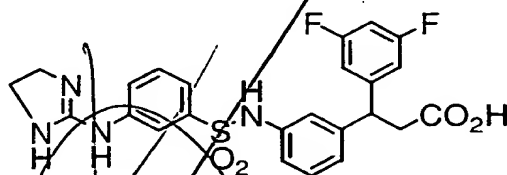
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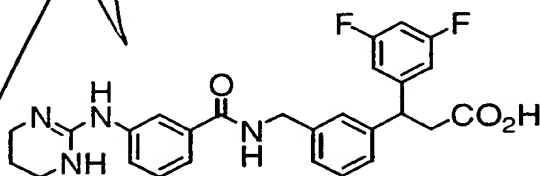
(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-D-alanine,

11)



b-[3-[[[3-[[4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]sulfonyl]amino]phenyl]-3,5-difluorobenzenepropanoic acid,

12)

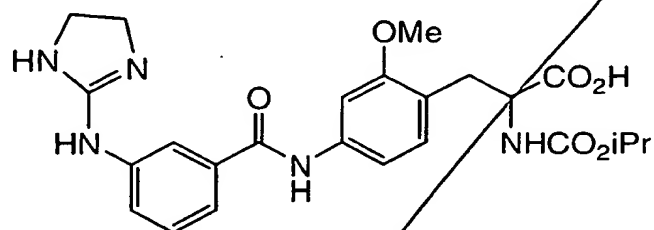


3,5-difluoro-b-[3-[[[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]benzoyl]amino]methyl]phenyl]benzenepropanoic acid,

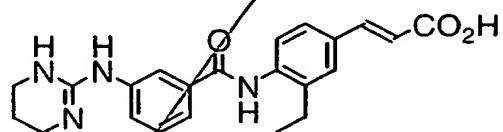
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13)



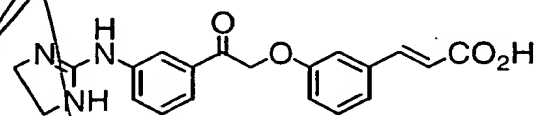
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(2E)-3-[3-ethyl-4-[[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]benzoyl]amino]phenyl]-2-propenoic acid,

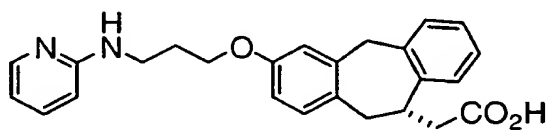
15)



10

(2E)-3-[3-[2-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]-2-oxoethoxy]phenyl]-2-propenoic acid,

16)

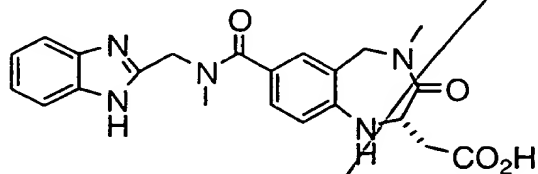


15

(10S)-10,11-dihydro-3-[3-(2-pyridinylamino)propoxy]-5H-dibenzo[a,d]cycloheptene-10-acetic acid,

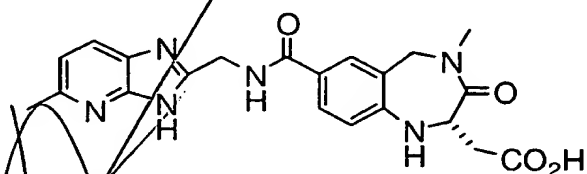
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17)



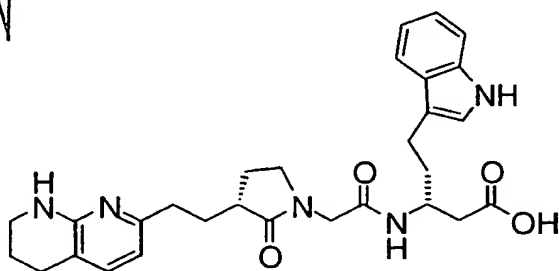
(2S)-7-[[[(1H-benzimidazol-2-ylmethyl)methylamino]carbonyl]-2,3,4,5-tetrahydro-4-methyl-3-oxo-1H-1,4-benzodiazepine-2-acetic acid,

18)



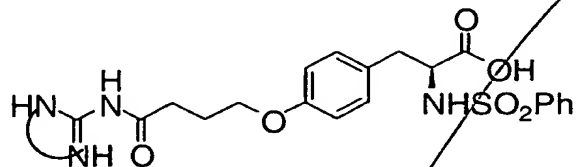
(2S)-2,3,4,5-tetrahydro-4-methyl-7-[[[(5-methyl-1H-imidazo[4,5-b]pyridin-2-yl)methyl]amino]carbonyl]-3-oxo-1H-1,4-benzodiazepine-2-acetic acid,

19)

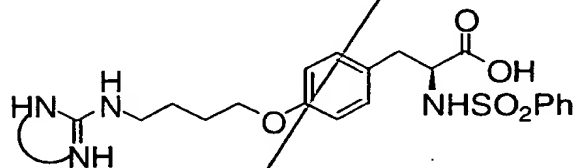


(bR)-b-[[[(3R)-2-oxo-3-[2-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)ethyl]-1-pyrrolidinyl]acetyl]amino]-1H-indole-3-pentanoic acid,

20)

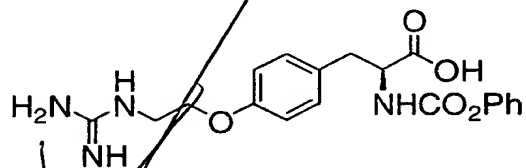


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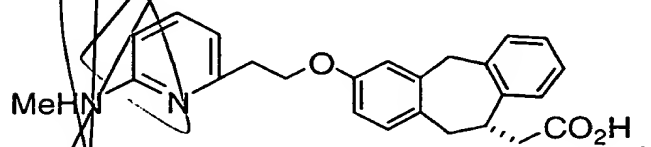


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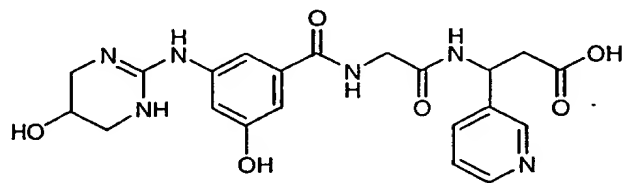


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24) Vitaxin antibody(Ixsys),

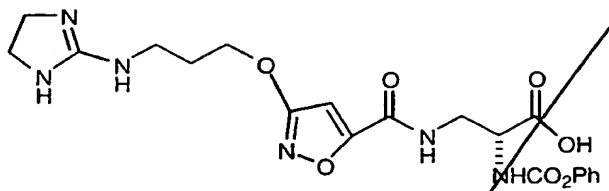
25) Merck KGaA EMD-121974, cyclo[RGDf-N(Me)V-],

26)

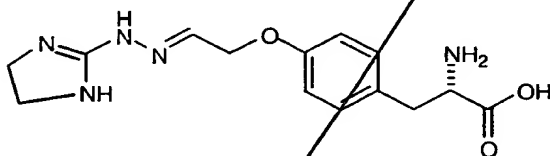


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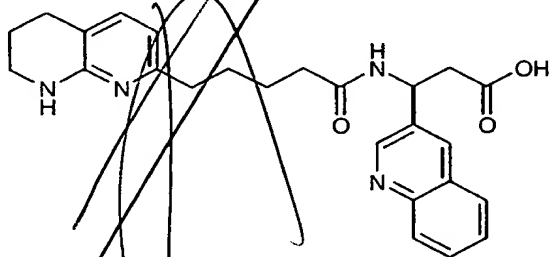
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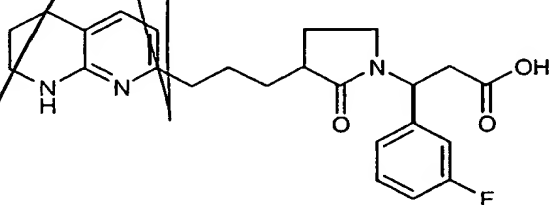
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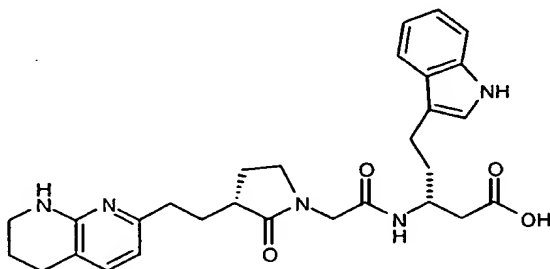
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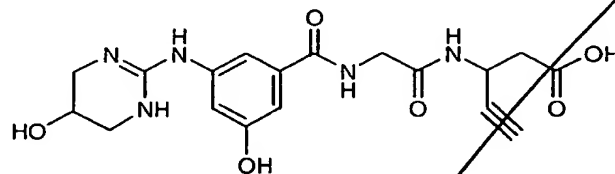


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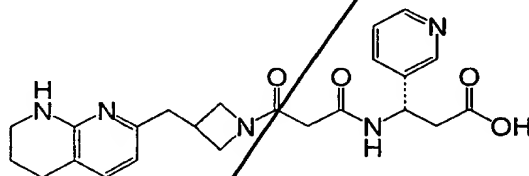
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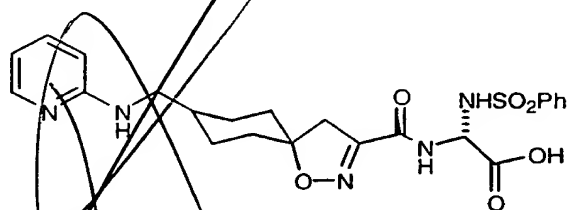
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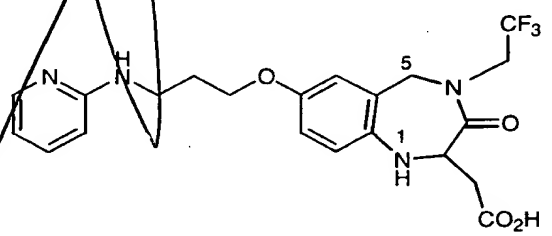
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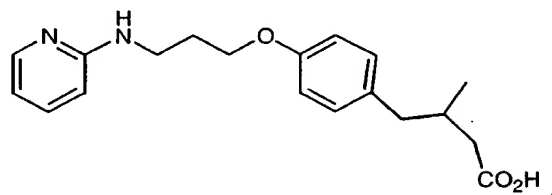
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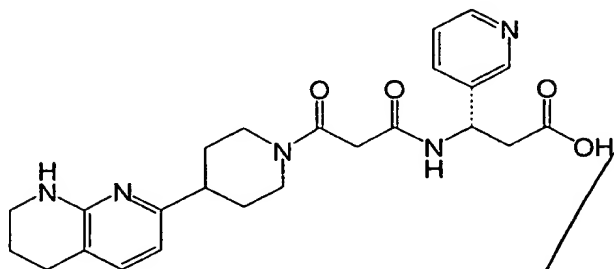
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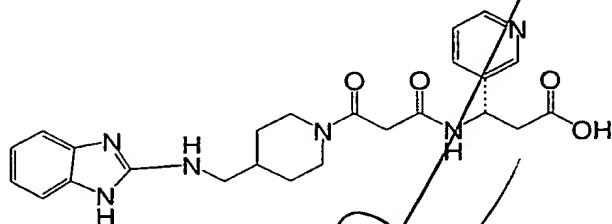
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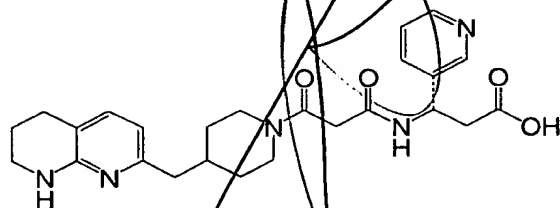
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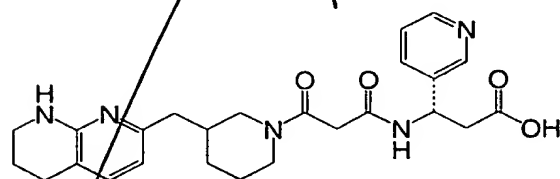
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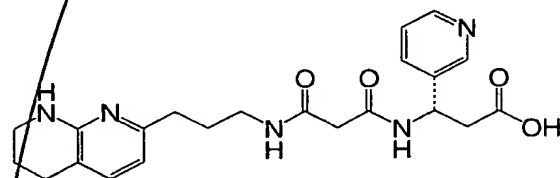
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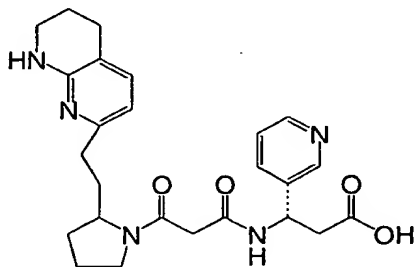


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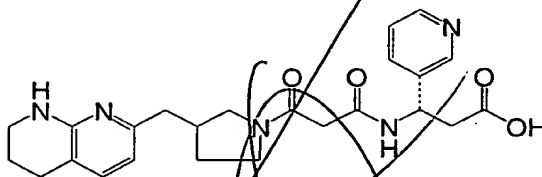
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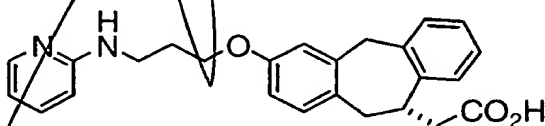


and

43)

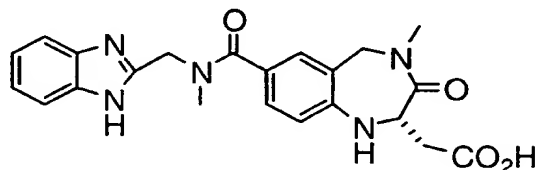


5 37. The method of Claim 1 wherein the integrin antagonist is



10 (10S)-10,11-dihydro-3-[3-(2-pyridinylamino)propoxy]-5H-dibenzo[a,d]cycloheptene-10-acetic acid.

38. The method of Claim 1 wherein the integrin antagonist is

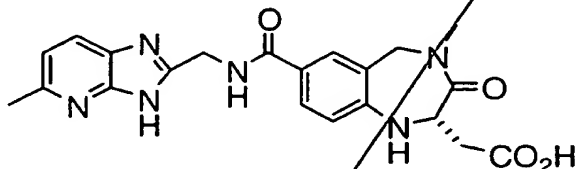


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(2S)-7-[[[(1H-benzimidazol-2-ylmethyl)methylamino]carbonyl]-2,3,4,5-tetrahydro-4-methyl-3-oxo-1H-1,4-benzodiazepine-2-acetic acid.

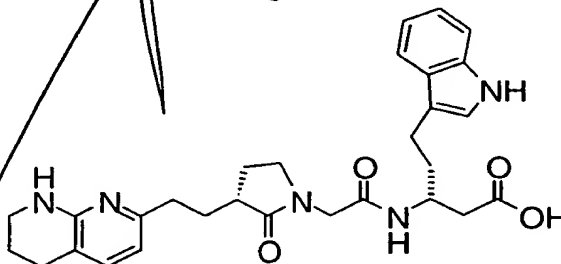
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39. The method of Claim 1 wherein the integrin antagonist is



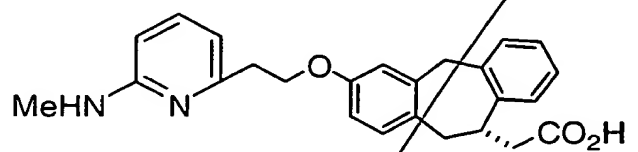
(2S)-2,3,4,5-tetrahydro-4-methyl-7-[[[(5-methyl-1H-imidazo[4,5-b]pyridin-2-yl)methyl]amino]carbonyl]-3-oxo-1H-1,4-benzodiazepine-2-acetic acid.

40. The method of Claim 1 wherein the integrin antagonist is



(bR)-b-[[[(3R)-2-oxo-3-[2-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)ethyl]-1-pyrrolidinyl]acetyl]amino]-1H-indole-3-pentanoic acid.

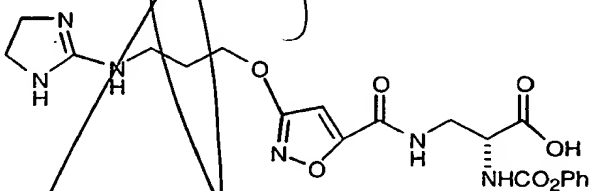
41. The method of Claim 1 wherein the integrin antagonist is



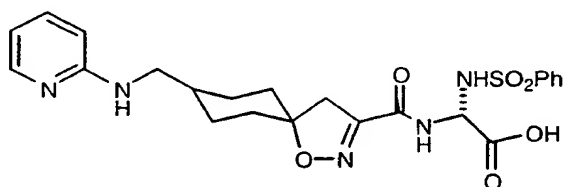
5 42. The method of Claim 1 wherein the integrin antagonist is Vitaxin antibody(Ixsys).

43. The method of Claim 1 wherein the integrin antagonist is Merck KGaA EMD-121974, cyclo[RGDf-N(Me)V-]

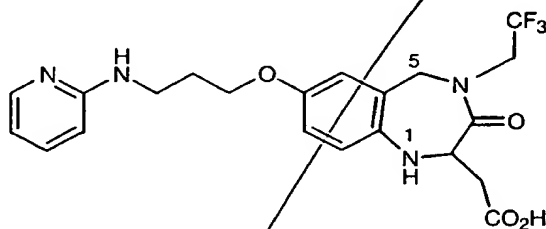
10 44. The method of Claim 1 wherein the integrin antagonist is



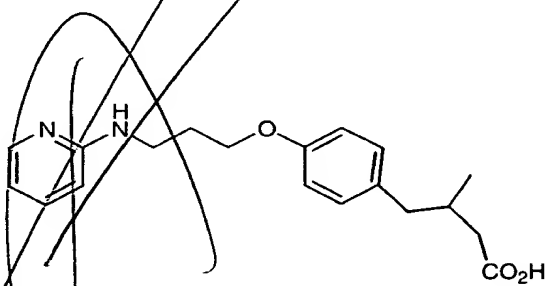
15 45. The method of Claim 1 wherein the integrin antagonist is



46. The method of Claim 1 wherein the integrin antagonist is



47. The method of Claim 1 wherein the integrin antagonist is



48. The method of Claim 1 wherein the neoplasia is selected from the group consisting of lung cancer, breast cancer, gastrointestinal cancer, bladder cancer, head and neck cancer and cervical cancer.

49. The method of Claim 1 wherein the neoplasia is selected from the group consisting of acral lentiginous melanoma, actinic keratoses, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, bronchial gland carcinomas, capillary, carcinoids, carcinoma, carcinosarcoma, cavernous, cholangiocarcinoma, chondrosarcoma, choriod plexus papilloma/carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial

hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal, epitheloid, Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumors, glioblastoma, glucagonoma,

5 hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatocellular carcinoma, insulinoma, intraepithelial neoplasia, interepithelial squamous cell neoplasia, invasive squamous cell carcinoma, large cell carcinoma,

10 leiomyosarcoma, lentigo maligna melanomas, malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal, mesothelial, metastatic carcinoma, mucoepidermoid carcinoma, neuroblastoma, neuroepithelial adenocarcinoma nodular

15 melanoma, oat cell carcinoma, oligodendroglial, osteosarcoma, pancreatic polypeptide, papillary serous adenocarcinoma, pineal cell, pituitary tumors, plasmacytoma, pseudosarcoma, pulmonary blastoma, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma,

20 sarcoma, serous carcinoma, small cell carcinoma, soft tissue carcinomas, somatostatin-secreting tumor, squamous carcinoma, squamous cell carcinoma, submesothelial, superficial spreading melanoma, undifferentiated carcinoma, uveal melanoma, verrucous

25 carcinoma, vipoma, well differentiated carcinoma, and Wilm's tumor.

50. A method for treating or preventing a neoplasia disorder in a mammal in need of such treatment or prevention, which method comprises administering to

30 said mammal a therapeutically-effective amount of a combination of radiation therapy, an integrin

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antagonist, and one or more antineoplastic agents, wherein said antineoplastic agents are selected from the group consisting of anastrozole, calcium carbonate, capecitabine, carboplatin, cisplatin, Cell Pathways CP-461, cyclophosphamide, docetaxel, doxorubicin, etoposide, fluorouracil (5-FU), fluoxymestrine, gemcitabine, goserelin, irinotecan, ketoconazole, letrozol, leucovorin, levamisole, megestrol, mitoxantrone, paclitaxel, raloxifene, retinoic acid, tamoxifen, thiotepa, topotecan, toremifene, vinorelbine, vinblastine, vincristine, selenium (selenomethionine), ursodeoxycholic acid, sulindac sulfone and eflornithine (DFMO).

51. The method of Claim 50 wherein the combination is administered in a sequential manner.

52. The method of Claim 50 wherein the combination is administered in a substantially simultaneous manner.

53. The method of Claim 50 wherein the antineoplastic agent is capecitabine.

54. The method of Claim 50 wherein the antineoplastic agent is carboplatin.

55. The method of Claim 50 wherein the antineoplastic agent is cisplatin.

56. The method of Claim 50 wherein the antineoplastic agent is Cell Pathways CP-461.

57. The method of Claim 50 wherein the antineoplastic agent is docetaxel.

58. The method of Claim 50 wherein the antineoplastic agent is doxorubicin.

59. The method of Claim 50 wherein the antineoplastic agent is etoposide.

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60. The method of Claim 50 wherein the antineoplastic agent is fluorouracil (5-FU).

61. The method of Claim 50 wherein the antineoplastic agent is fluoxymestrine.

5 62. The method of Claim 50 wherein the antineoplastic agent is gemcitabine.

63. The method of Claim 50 wherein the antineoplastic agent is goserelin.

10 64. The method of Claim 50 wherein the antineoplastic agent is irinotecan.

65. The method of Claim 50 wherein the antineoplastic agent is ketoconazole.

66. The method of Claim 50 wherein the antineoplastic agent is letrozol.

15 67. The method of Claim 50 wherein the antineoplastic agent is leucovorin.

68. The method of Claim 50 wherein the antineoplastic agent is levamisole.

20 69. The method of Claim 50 wherein the antineoplastic agent is megestrol.

70. The method of Claim 50 wherein the antineoplastic agent is mitoxantrone.

71. The method of Claim 50 wherein the antineoplastic agent is paclitaxel.

25 72. The method of Claim 50 wherein the antineoplastic agent is raloxifene.

73. The method of Claim 50 wherein the antineoplastic agent is retinoic acid.

30 74. The method of Claim 50 wherein the antineoplastic agent is tamoxifen.

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75. The method of Claim 50 wherein the antineoplastic agent is thiotepa.

76. The method of Claim 50 wherein the antineoplastic agent is topotecan.

5 77. The method of Claim 50 wherein the antineoplastic agent is toremifene.

78. The method of Claim 50 wherein the antineoplastic agent is vinorelbine.

10 79. The method of Claim 50 wherein the antineoplastic agent is vinblastine.

80. The method of Claim 50 wherein the antineoplastic agent is vincristine.

81. The method of Claim 50 wherein the antineoplastic agent is selenium (selenomethionine).

15 82. The method of Claim 50 wherein the antineoplastic agent is sulindac sulfone.

83. The method of Claim 50 wherein the antineoplastic agent is ursodeoxycholic acid.

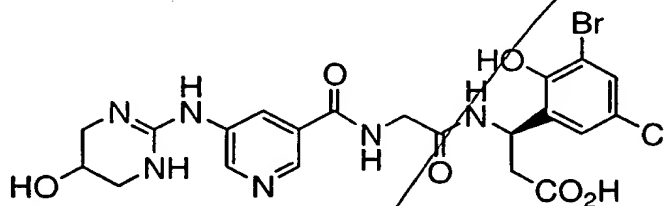
20 84. The method of Claim 50 wherein the antineoplastic agent is eflornithine (DFMO).

85. The method of Claim 50 wherein the integrin antagonist is selected from compounds, and their pharmaceutically acceptable salts thereof, of the group consisting of:

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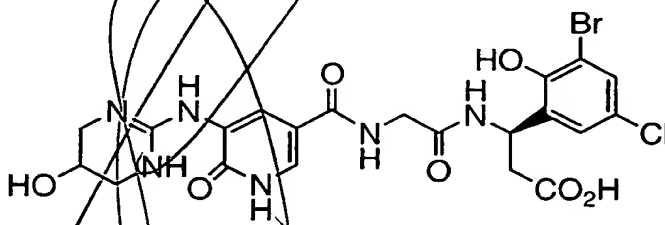
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1)



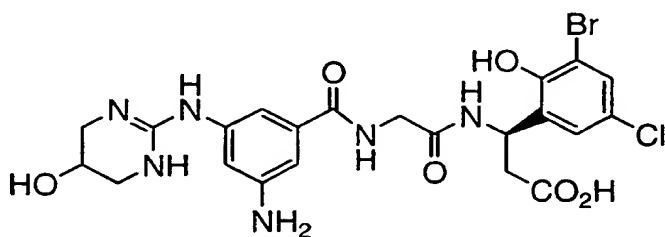
(3R)-N-[[5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

2)



(3R)-N-[[1,6-dihydro-6-oxo-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

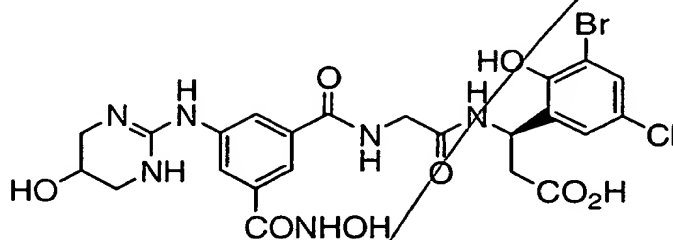
3)



(3R)-N-[3-amino-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

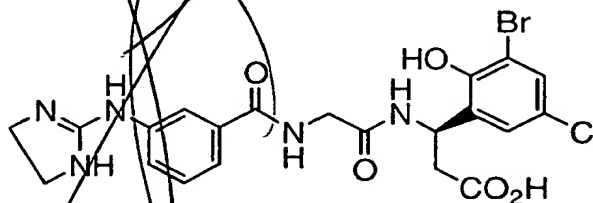
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4)



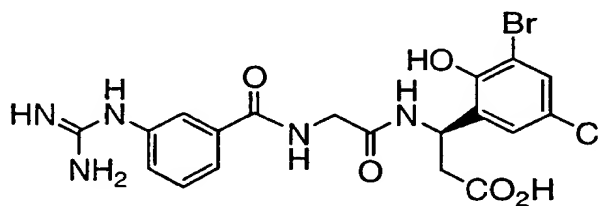
(3R)-N-[3-[(hydroxyamino)carbonyl]-5-
 [(1,4,5,6-tetrahydro-5-hydroxy)-2-
 pyrimidinyl]amino]benzoyl]glycyl-3-(3-bromo-5-
 chloro-2-hydroxyphenyl)-b-alanine,

5)



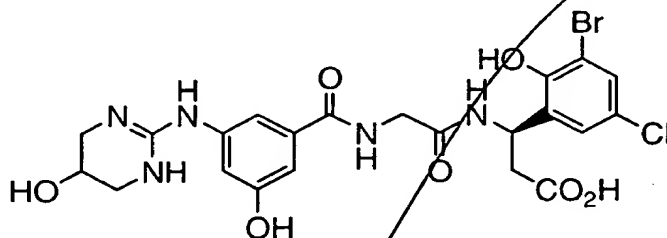
(3R)-N-[3-[(4,5-dihydro-1H-imidazol-2-
 yl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-
 hydroxyphenyl)-b-alanine,

6)



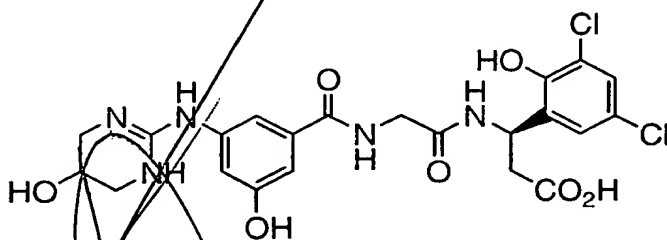
(3R)-N-[3-
 [(aminoiminomethyl)amino]benzoyl]glycyl-3-(3-
 bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

7)



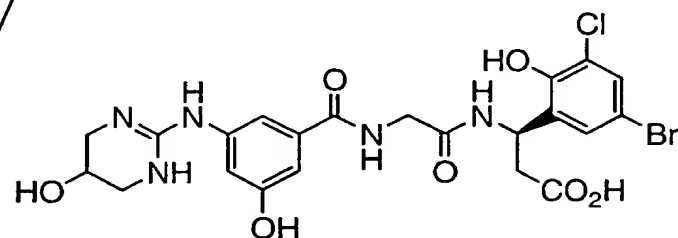
(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

8)



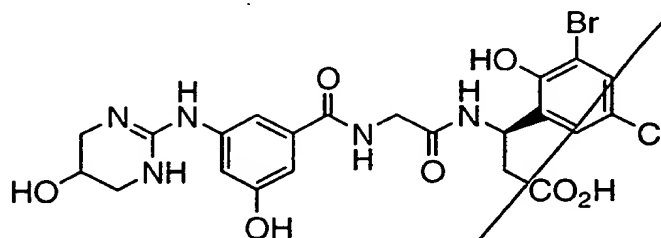
(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3,5-dichloro-2-hydroxyphenyl)-b-alanine,

9)



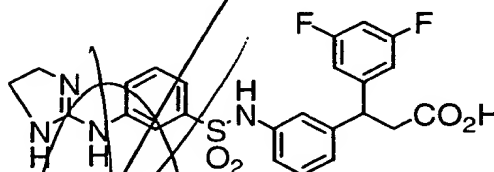
(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(5-bromo-3-chloro-2-hydroxyphenyl)-b-alanine,

10)



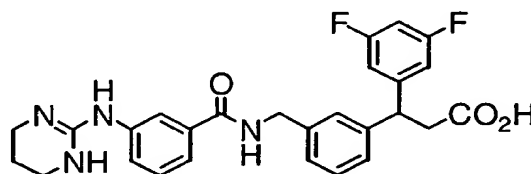
(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

11)



b-[3-[[[3-[[4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]sulfonyl]amino]phenyl]-3,5-difluorobenzenepropanoic acid,

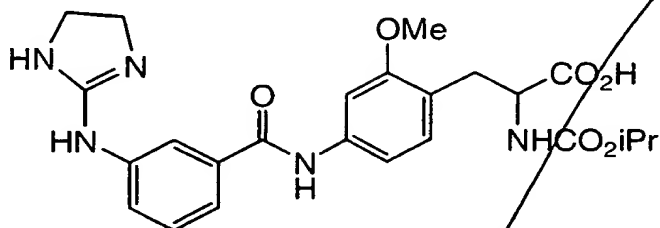
12)



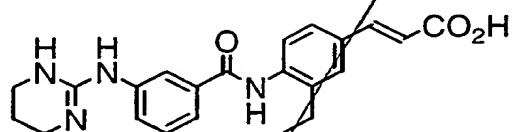
3,5-difluoro-b-[3-[[[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]benzoyl]amino]methyl]phenyl]benzenepropanoic acid,

-195-

13)



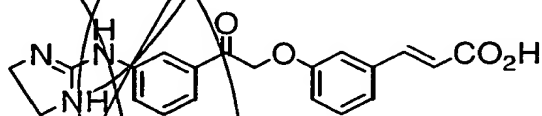
14)



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(2E)-3-[3-ethyl-4-[[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]benzoyl]amino]phenyl]-2-propenoic acid,

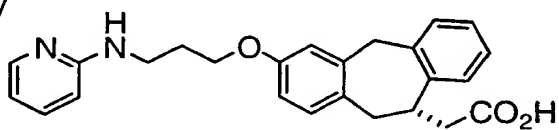
15)



10

(2E)-3-[3-[2-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]-2-oxoethoxy]phenyl]-2-propenoic acid,

16)

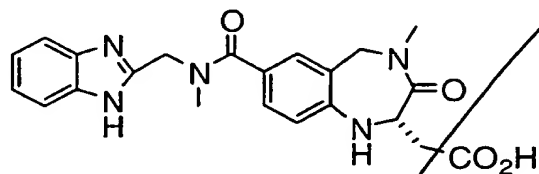


15

(10S)-10,11-dihydro-3-[3-(2-pyridinylamino)propoxy]-5H-dibenzo[a,d]cycloheptene-10-acetic acid,

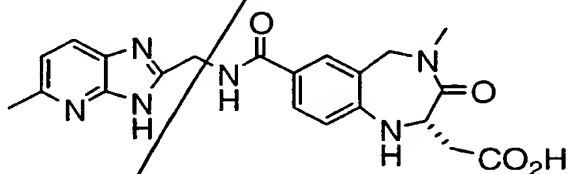
T0500T"46625860

17)



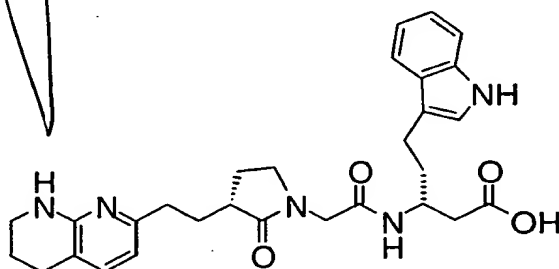
(2S)-7-[[[(1H-benzimidazol-2-ylmethyl)methylamino]carbonyl]-2,3,4,5-tetrahydro-4-methyl-3-oxo-1H-1,4-benzodiazepine-2-acetic acid,

18)



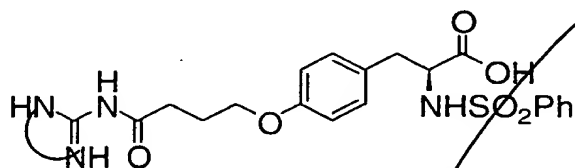
(2S)-2,3,4,5-tetrahydro-4-methyl-7-[[[(5-methyl-1H-imidazo[4,5-b]pyridin-2-yl)methyl]amino]carbonyl]-3-oxo-1H-1,4-benzodiazepine-2-acetic acid,

19)

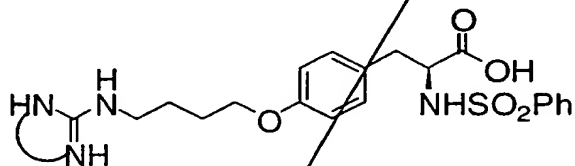


(bR)-b-[[[(3R)-2-oxo-3-[2-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)ethyl]-1-pyrrolidinyl]acetyl]amino]-1H-indole-3-pentanoic acid,

20)

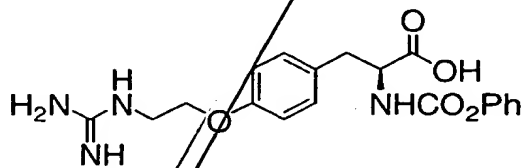


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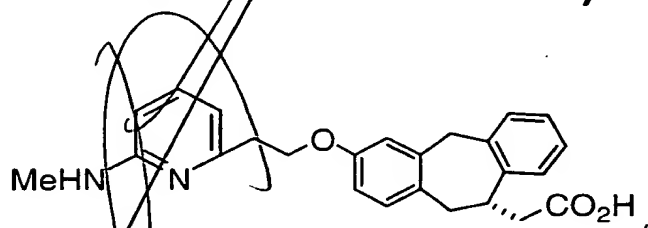


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22)



23)

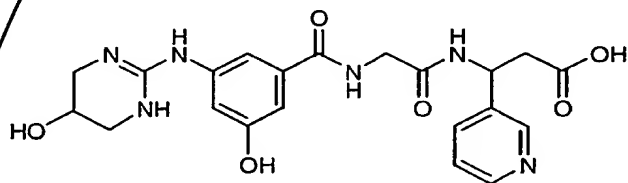


10

24) Vitaxin antibody(Ixsy),

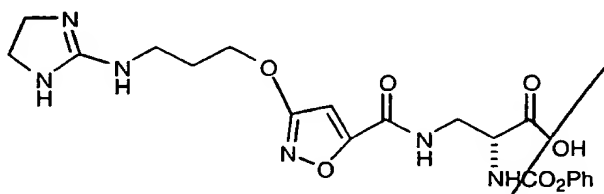
25) Merck KGaA EMD-121974, cyclo[RGDf-N(Me)V-],

26)

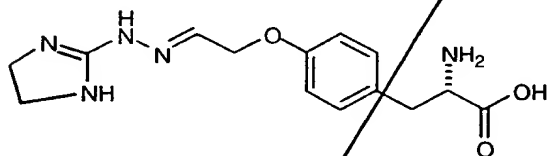


-198-

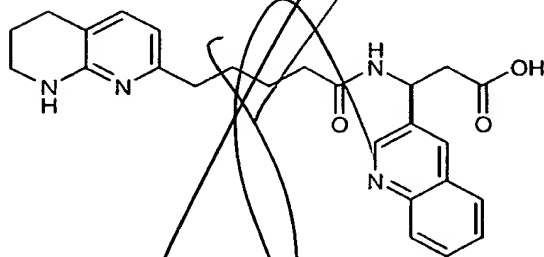
27)



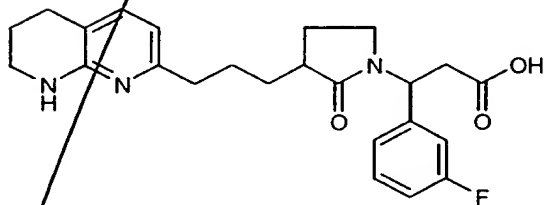
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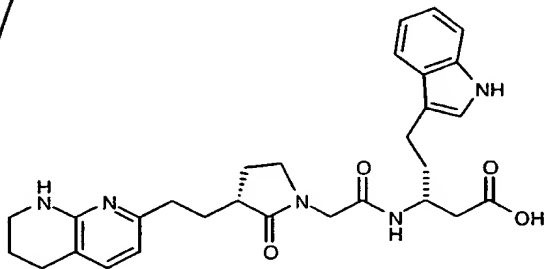
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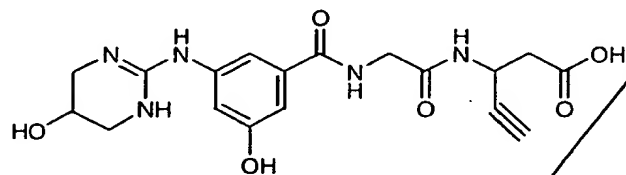


30)

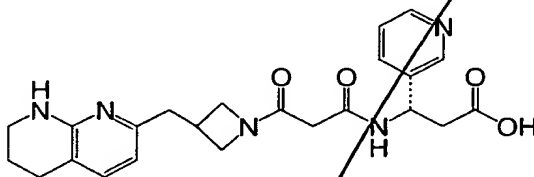


31)

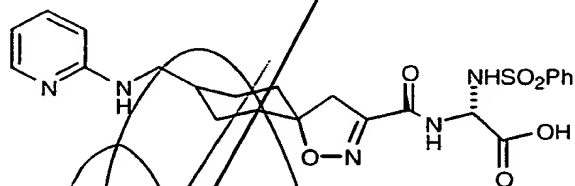




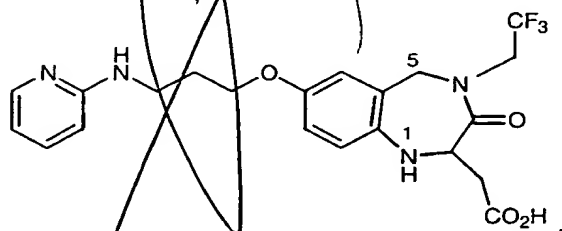
33)



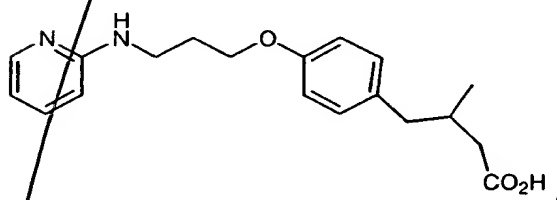
34)



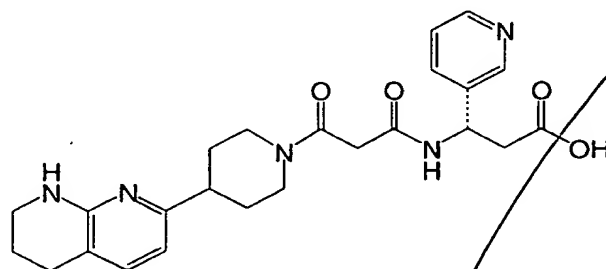
35)



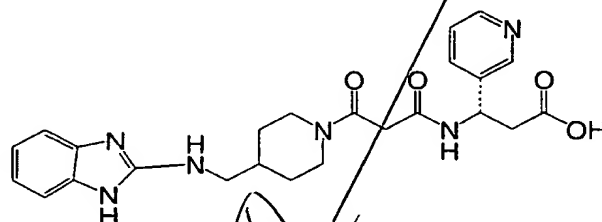
36)



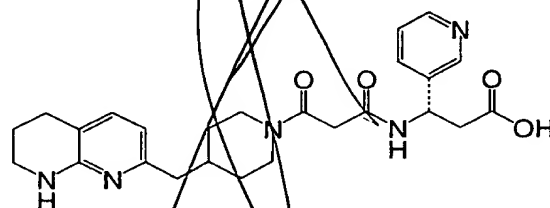
37)



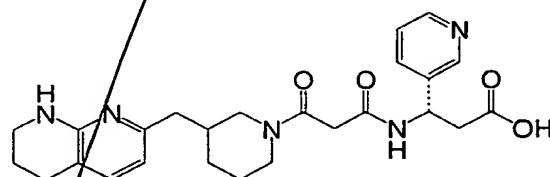
38)



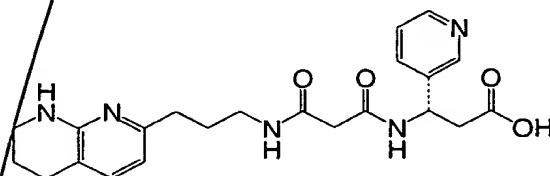
39)



40)



41)

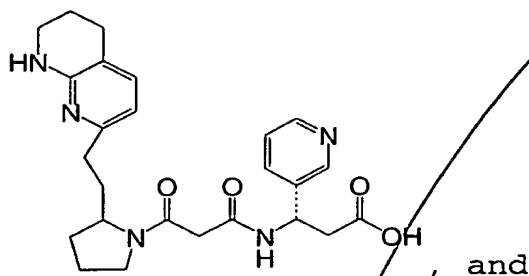


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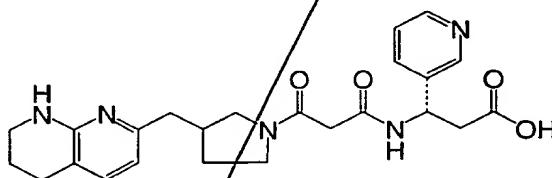
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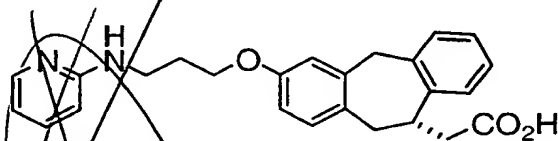
42)



43)



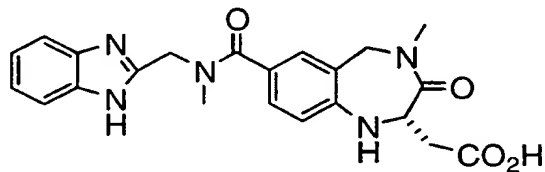
- 5 86. The method of Claim 50 wherein the integrin antagonist is



10

(10S)-10,11-dihydro-3-[3-(2-pyridinylamino)propoxy]-5H-dibenzo[a,d]cycloheptene-10-acetic acid.

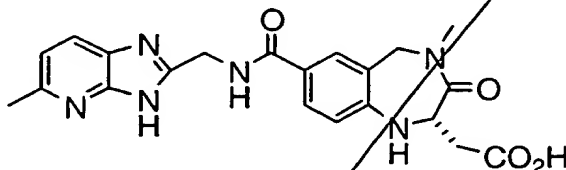
87. The method of Claim 50 wherein the integrin antagonist is



15

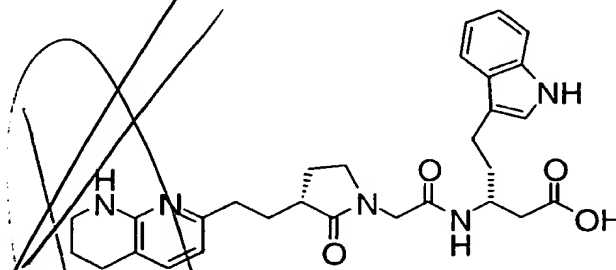
(2S)-7-[[[(1H-benzimidazol-2-ylmethyl)methylamino]carbonyl]-2,3,4,5-tetrahydro-4-methyl-3-oxo-1H-1,4-benzodiazepine-2-acetic acid.

88. The method of Claim 50 wherein the integrin antagonist is



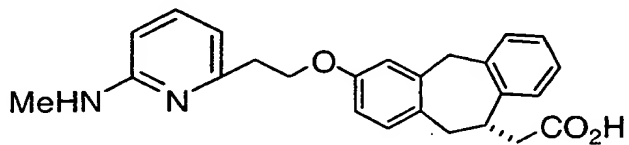
5 (2S)-2,3,4,5-tetrahydro-4-methyl-7-[[[(5-methyl-1H-imidazo[4,5-b]pyridin-2-yl)methyl]amino]carbonyl]-3-oxo-1H-1,4-benzodiazepine-2-acetic acid.

89. The method of Claim 50 wherein the integrin antagonist is



10 (bR)-b-[[[(3R)-2-oxo-3-[2-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)ethyl]-1-pyrrolidinyl]acetyl]amino]-1H-indole-3-pentanoic acid.

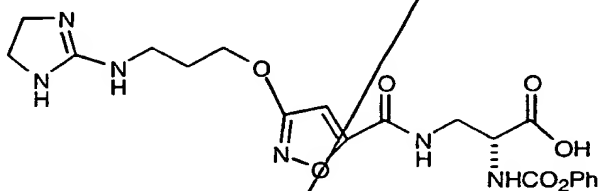
15 90. The method of Claim 50 wherein the integrin antagonist is



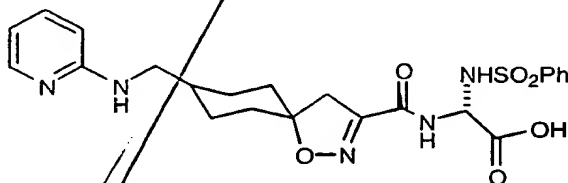
91. The method of Claim 50 wherein the integrin antagonist is Vitaxin antibody(Ixsys).

92. The method of Claim 50 wherein the integrin antagonist is Merck KGaA EMD-121974, cyclo[RGDf-N(Me)V-].

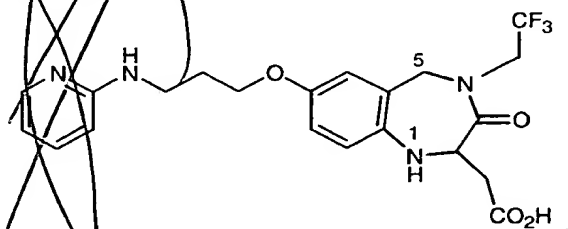
93. The method of Claim 50 wherein the integrin antagonist is



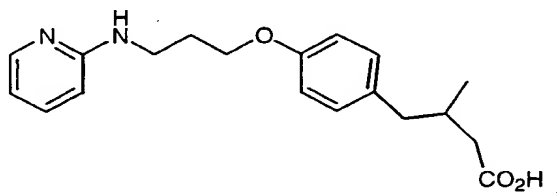
94. The method of Claim 50 wherein the integrin antagonist is



95. The method of Claim 50 wherein the integrin antagonist is



96. The method of Claim 50 wherein the integrin antagonist is



97. The method of Claim 50 wherein the neoplasia is selected from the group consisting of lung cancer,

breast cancer, gastrointestinal cancer, bladder cancer, head and neck cancer and cervical cancer.

98. The method of Claim 50 wherein the neoplasia is selected from the group consisting of acral
- 5 lentiginous melanoma, actinic keratoses, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, astrocytic tumors, Bartholin gland carcinoma, basal cell carcinoma, bronchial gland carcinomas, capillary, carcinoids, carcinoma,
- 10 carcinosarcoma, cavernous, cholangiocarcinoma, chondrosarcoma, choroid plexus papilloma/carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal, epitheloid,
- 15 Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumors, glioblastoma, glucagonoma, hemangioblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatocellular carcinoma, insulinoma, intraepithelial
- 20 neoplasia, interepithelial squamous cell neoplasia, invasive squamous cell carcinoma, large cell carcinoma, leiomyosarcoma, lentigo maligna melanomas, malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal, mesothelial,
- 25 metastatic carcinoma, mucoepidermoid carcinoma, neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, oat cell carcinoma, oligodendroglial, osteosarcoma, pancreatic polypeptide, papillary serous adenocarcinoma, pineal cell, pituitary tumors,
- 30 plasmacytoma, pseudosarcoma, pulmonary blastoma, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma,

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sarcoma, serous carcinoma, small cell carcinoma, soft tissue carcinomas, somatostatin-secreting tumor, squamous carcinoma, squamous cell carcinoma, submesothelial, superficial spreading melanoma, undifferentiated carcinoma, uveal melanoma, verrucous carcinoma, vipoma, well differentiated carcinoma, and Wilm's tumor.

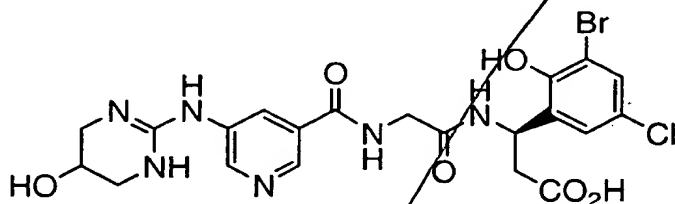
99. A combination comprising an integrin antagonist and one or more antineoplastic agents, wherein said antineoplastic agents are selected from the group consisting of anastrozole, calcium carbonate, capecitabine, carboplatin, cisplatin, Cell Pathways CP-461, cyclophosphamide, docetaxel, doxorubicin, etoposide, fluorouracil (5-FU), fluoxymestrine, gemcitabine, goserelin, irinotecan, ketoconazole, letrozol, leucovorin, levamisole, megestrol, mitoxantrone, paclitaxel, raloxifene, retinoic acid, tamoxifen, thiotepa, topotecan, toremifene, vinorelbine, vinblastine, vincristine, selenium (selenomethionine), ursodeoxycholic acid, sulindac sulfone and eflornithine (DFMO).

100. The combination of Claim 99 wherein the integrin antagonist is selected from compounds, and their pharmaceutically acceptable salts thereof, of the group consisting of:

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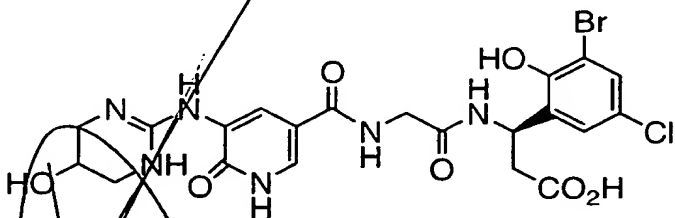
-206-

1)



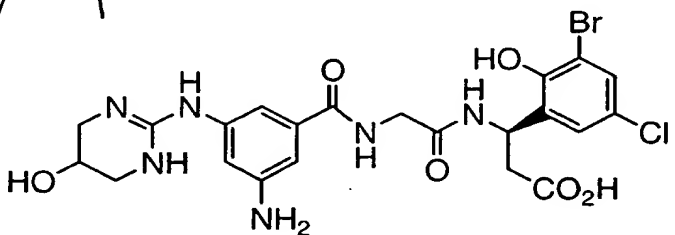
(3R)-N-[[5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

2)



(3R)-N-[[1,5-dihydro-6-oxo-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]-3-pyridinyl]carbonyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

3)

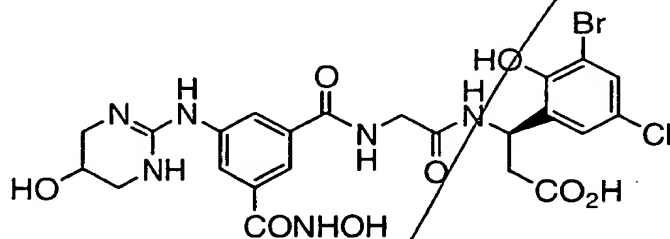


(3R)-N-[3-amino-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

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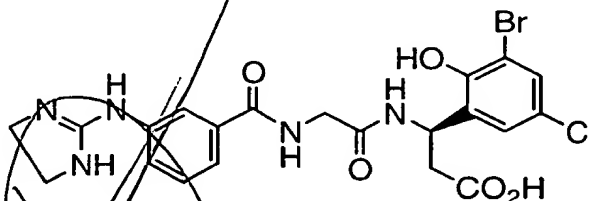
-207-

4)



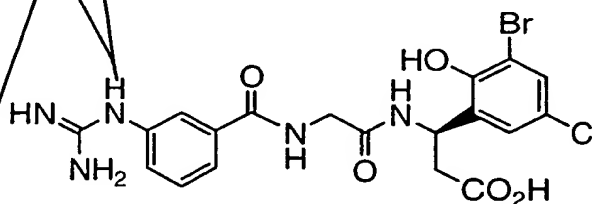
(3R)-N-[3-[(hydroxyamino)carbonyl]-5-
 [(1,4,5,6-tetrahydro-5-hydroxy)-2-
 5 pyrimidinyl]amino]benzoyl]glycyl-3-(3-bromo-5-
 chloro-2-hydroxyphenyl)-b-alanine,

5)



(3R)-N-[3-[(4,5-dihydro-1H-imidazol-2-
 10 yl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-
 hydroxyphenyl)-b-alanine,

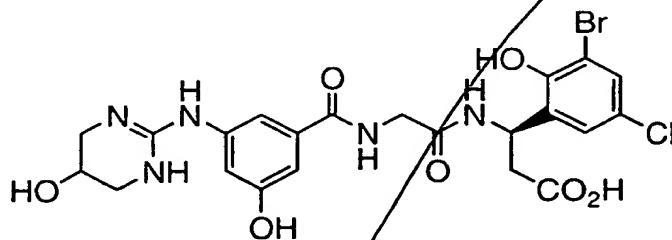
6)



(3R)-N-[3-
 15 [(aminoiminomethyl)amino]benzoyl]glycyl-3-(3-
 bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

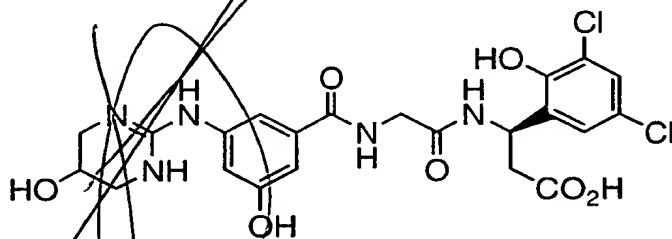
T05007-466/5860

7)



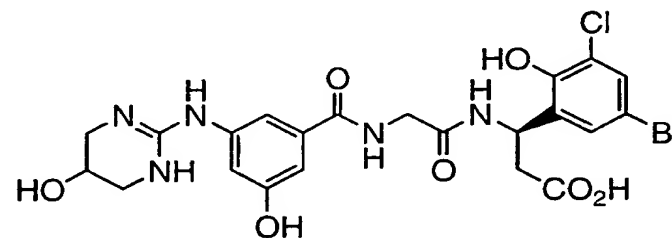
(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-b-alanine,

8)



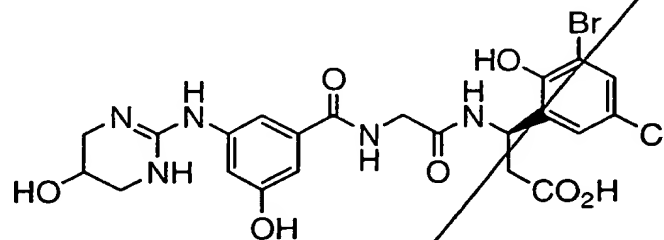
(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3,5-dichloro-2-hydroxyphenyl)-b-alanine,

9)



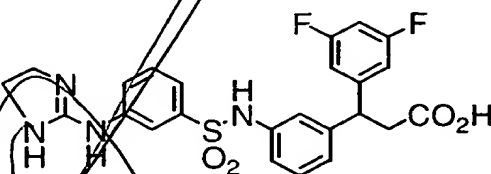
(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(5-bromo-3-chloro-2-hydroxyphenyl)-b-alanine,

10)



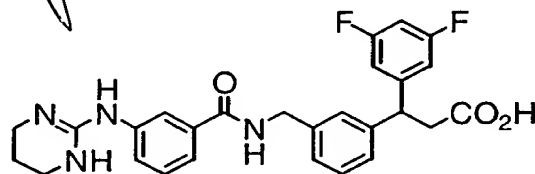
(3R)-N-[3-hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino]benzoyl]glycyl-3-(3-bromo-5-chloro-2-hydroxyphenyl)-L-alanine,

11)



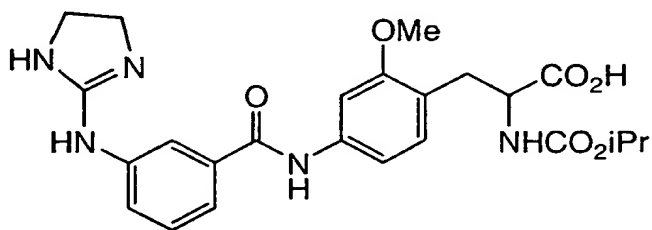
b-[3-[[[3-[[4/5-dihydro-1H-imidazol-2-yl)amino]phenyl]sulfonyl]amino]phenyl]-3,5-difluorobenzenepropanoic acid,

12)



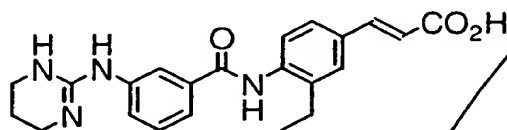
3,5-difluoro-b-[3-[[[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]benzoyl]amino]methyl]phenyl]benzenepropanoic acid,

13)



14)

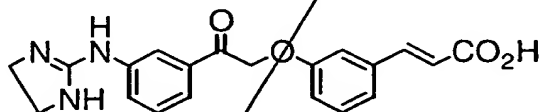
-210-



(2E)-3-[3-ethyl-4-[[3-[(1,4,5,6-tetrahydro-2-pyrimidinyl)amino]benzoyl]amino]phenyl]-2-propenoic acid,

5

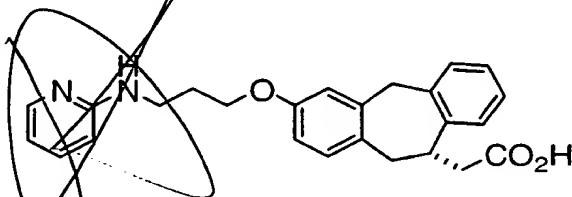
15)



(2E)-3-[3-[2-[3-[(4,5-dihydro-1H-imidazol-2-yl)amino]phenyl]-2-oxoethoxy]phenyl]-2-propenoic acid,

10

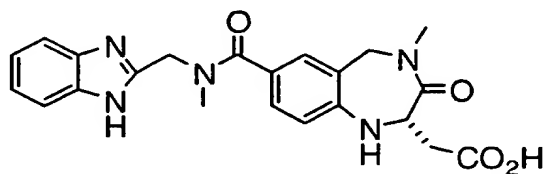
16)



(10S)-10,11-dihydro-3-[3-(2-pyridinylamino)propoxy]-5H-dibenzo[a,d]cycloheptene-10-acetic acid,

15

17)



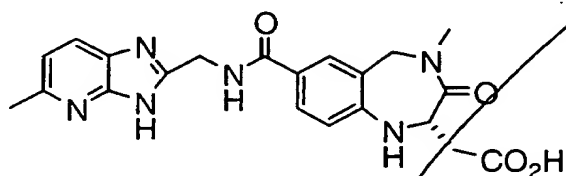
(2S)-7-[[[(1H-benzimidazol-2-ylmethyl)methylamino]carbonyl]-2,3,4,5-tetrahydro-4-methyl-3-oxo-1H-1,4-benzodiazepine-2-acetic acid,

20

18)

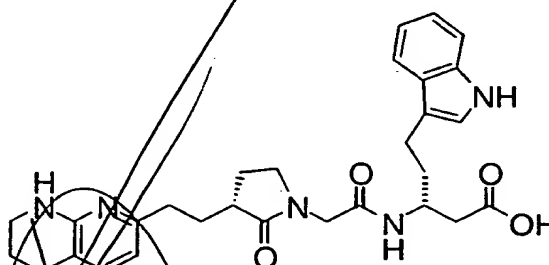
T0500T-46625860

-211-



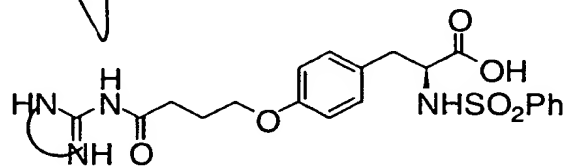
(2S)-2,3,4,5-tetrahydro-4-methyl-7-[[[(5-methyl-1H-imidazo[4,5-b]pyridin-2-yl)methyl]amino]carbonyl]-3-oxo-1H-1,4-benzodiazepine-2-acetic acid,

19)

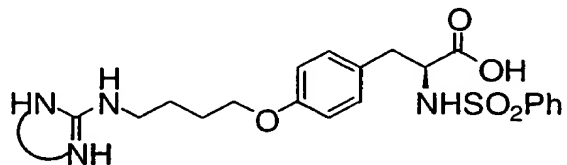


(bR)-b-[[[(3R)-2-oxo-3-[2-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)ethyl]-1-pyrrolidinyl]acetyl]amino]-1H-indole-3-pentanoic acid,

20)



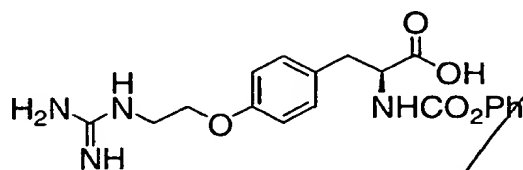
21)



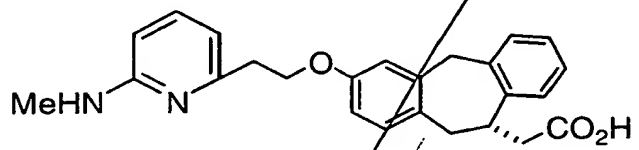
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22)



23)

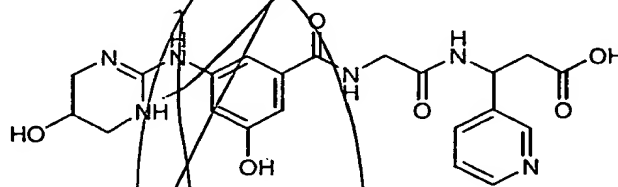


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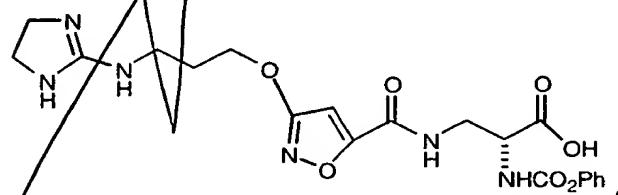
24) Vitaxin antibody (Ixsys),

25) Merck KGaA EMD-121974, cyclo[RGDf-N(Me)V-],

26)

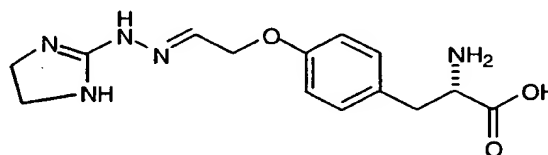


27)



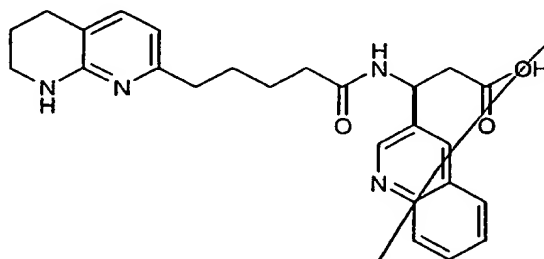
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28)

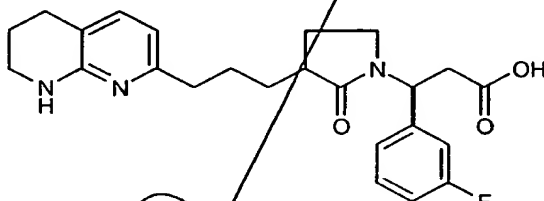


-213-

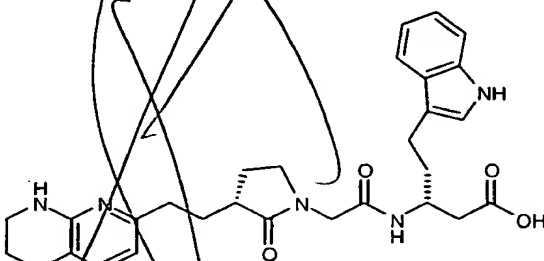
29)



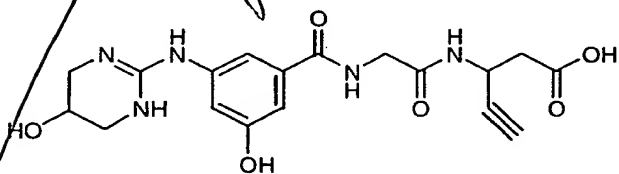
30)



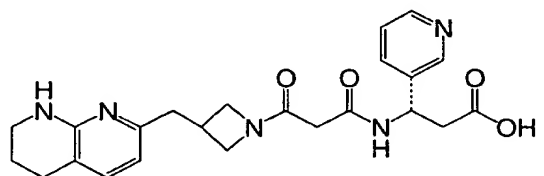
31)



32)

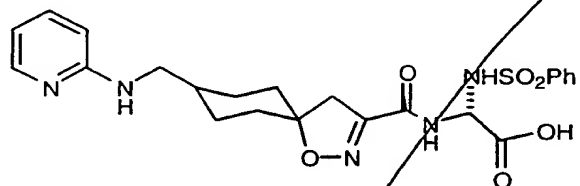


33)

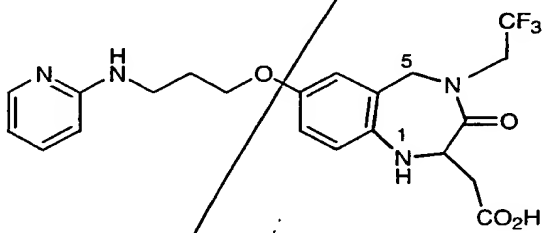


-214-

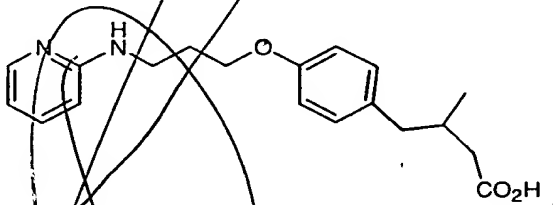
34)



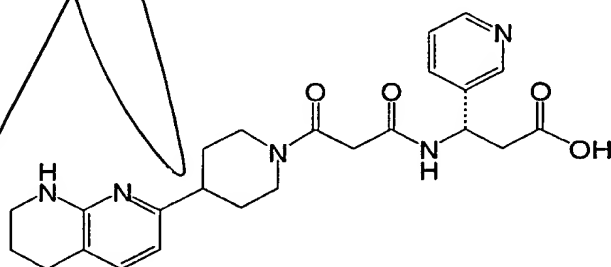
35)



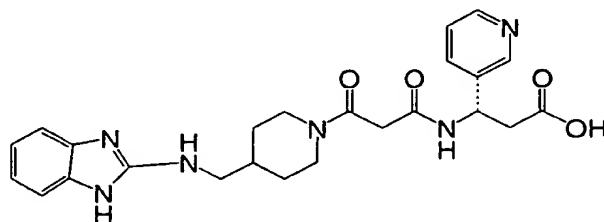
36)



37)



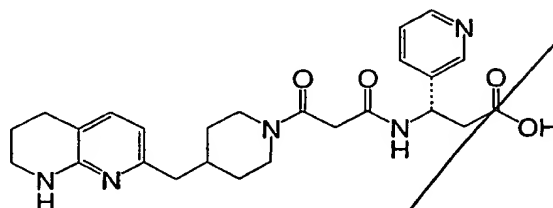
38)



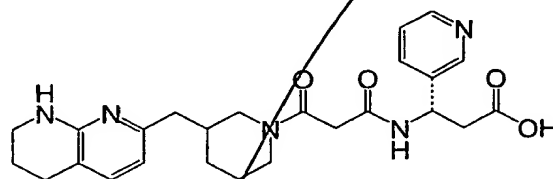
T05007-46625860

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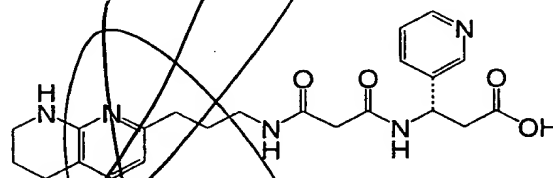
39)



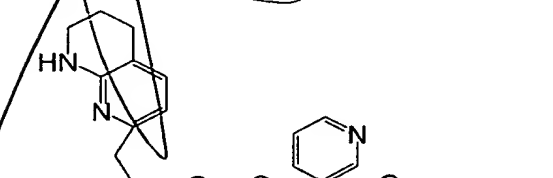
40)



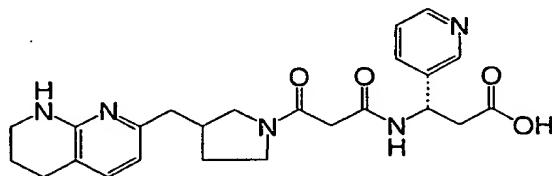
41)



42)

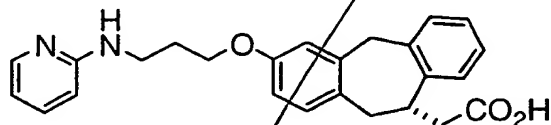


43)



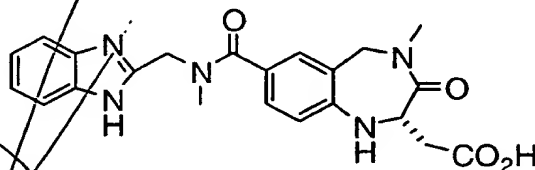
, and

101. The combination of Claim 99 wherein the integrin antagonist is



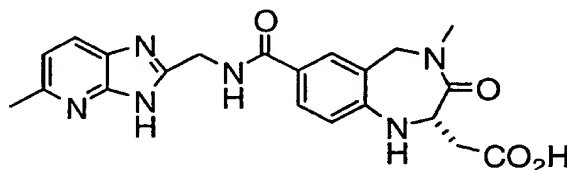
5 (10S)-10,11-dihydro-3-[3-(2-pyridinylamino)propoxy]-5H-dibenzo[a,d]cycloheptene-10-acetic acid.

102. The combination of Claim 99 wherein the integrin antagonist is



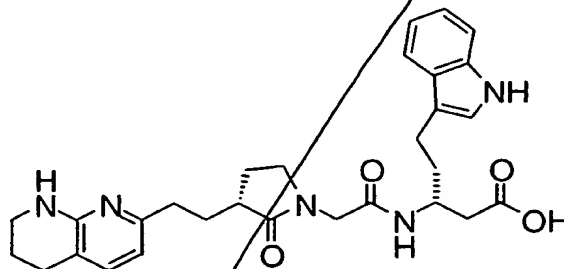
10 (2S)-7-[[[1H-benzimidazol-2-ylmethyl]methylamino]carbonyl]-2,3,4,5-tetrahydro-4-methyl-3-oxo-1H-1,4-benzodiazepine-2-acetic acid.

15 103. The combination of Claim 99 wherein the integrin antagonist is



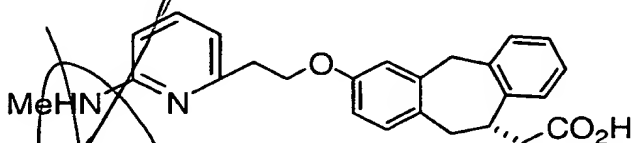
20 (2S)-2,3,4,5-tetrahydro-4-methyl-7-[[[(5-methyl-1H-imidazo[4,5-b]pyridin-2-yl)methyl]amino]carbonyl]-3-oxo-1H-1,4-benzodiazepine-2-acetic acid.

104. The combination of Claim 99 wherein the integrin antagonist is



(bR)-b-[[[(3R)-2-oxo-3-[2-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)ethyl]-1-pyrrolidinyl]acetyl]amino]-1H-indole-3-pentanoic acid.

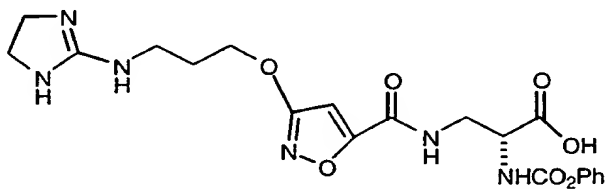
105. The combination of Claim 99 wherein the integrin antagonist is



106. The combination of Claim 99 wherein the integrin antagonist is Vitaxin antibody(Ixsys).

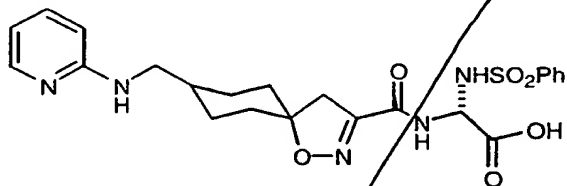
107. The combination of Claim 99 wherein the integrin antagonist is Merck KGaA EMD-121974, cyclo[RGDf-N(Me)V-].

108. The combination of Claim 99 wherein the integrin antagonist is

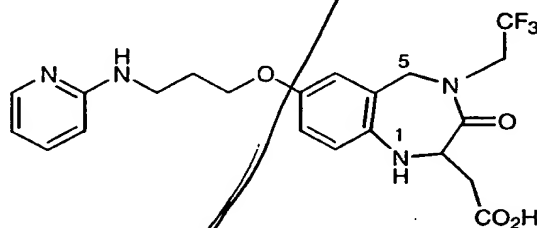


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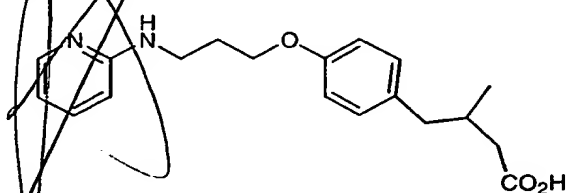
109. The combination of Claim 99 wherein the integrin antagonist is



110. The combination of Claim 99 wherein the integrin antagonist is



111. The combination of Claim 99 wherein the integrin antagonist is



112. The combination of Claim 1 wherein the antineoplastic agent is anastrozole.

113. The combination of Claim 1 wherein the antineoplastic agent is calcium carbonate.

114. The combination of Claim 50 wherein the antineoplastic agent is anastrozole.

115. The combination of Claim 50 wherein the antineoplastic agent is calcium carbonate.

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add
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